

## **GUIDELINES FOR DNA AND OTHER GENETIC-RELATED INFORMATION RESEARCH AT DVAMC**

### **Recommended definitions: (from the Genetic Information Nondiscrimination Act [GINA])**

**“Genetic research”** means human clinical or translational research involving genetic information or tests.

**“Genetic information”** means information about genetic tests, the genetic tests of family members, and the manifestation of a disease or disorder in family members (a “family member” is defined as a first-, second-, third-, or fourth-degree relative). It also includes any request for, or receipt of, genetic services, or participation in clinical research that includes genetic services, by an individual or his or her family members. “Genetic services” may include a genetic test, genetic counseling (including obtaining, interpreting, or assessing genetic information), or genetic education. The law states specifically that genetic information does not include information about sex or age.

**“Genetic test”** means an analysis of human DNA, RNA, chromosomes, proteins, or metabolites to detect genotypes, mutations, or chromosomal changes. However, according to the law, genetic test does not include:

- (i) an analysis of proteins or metabolites that does not detect genotypes, mutations, or chromosomal changes; or
- (ii) an analysis of proteins or metabolites that is directly related to a manifested disease, disorder, or pathological condition that could reasonably be detected by a healthcare professional with appropriate training and expertise in the field of medicine involved.”

### ***RECOMMENDATION #1: USE UNIFORM SAMPLE TERMINOLOGY***

In order to provide uniform terminology regarding the collection of tissue samples for use in clinical and translational research involving genetic technology, the DVAMC IRB recommends that DVAMC investigators use only the following terms in their consent forms and research protocols:

#### **A. DEIDENTIFIED Samples/specimens:**

Sometimes termed “anonymous” (unidentified) or “anonymized” (unlinkable); these are samples and specimens where identifiable information was not collected, or, if collected, was not maintained and cannot be retrieved. These samples lack any identifiers or codes that could link a particular sample to an identified specimen or a particular human being. Identification will never be possible, even by the original Principal Investigator who collected the data. The risk to the veteran’s welfare of involvement in this type of research is minimal.

**B. IDENTIFIABLE Samples/specimens:**

Sometimes termed “coded” or “linked”; these samples are identified by a code rather than with personally identifying information (e.g., name, SS#). This provides a high degree of confidentiality and makes it difficult, if not unlikely, that the person from whom the material was obtained would be identified unless results warrant disclosure or further contact--and the subject/patient gave previous consent for disclosure or contact. This applies to specimens that are sent to a third party for analysis or storage without identifiers if the key that can be used to identify (link) the samples to PHI exists (usually with the original study PI). The key file that links the specimens with the identifiers **MUST** be kept **ONLY** on the secure server behind the VA firewall (commonly termed S drive), and no paper copy is permitted. The risk to the veteran’s welfare of involvement in this type of research is greater than minimal, but significantly less than when samples are identified.

**C. IDENTIFIED Samples/specimens:**

These specimens are linked to personal information in such a way that the person from whom the material was obtained can be identified by name, patient number, or pedigree (i.e., his or her relationship to a family member whose identity is known). The identification would allow the researcher to link the biological information derived from the research directly to the individual from whom the material was obtained. The risk to the veteran’s welfare of involvement in this type of research is substantially greater than minimal, and this fact should be expressly mentioned in both verbal communications with the veteran and in the written consent documentation.

***RECOMMENDATION #2: ADHERE TO GUIDELINES FOR CONSENT FORMS AND PROCESSES INVOLVING DNA AND OTHER GENETIC-RELATED INFORMATION RESEARCH***

**A. PURPOSE**

Inform patients/participants clearly that sample(s) will be used for genetic research. Provide information or an overview of the possible risks and rewards relating to the research study in general and the specifics of the DNA or other genetic related information portion.

**B. COLLECTION, STORAGE, USE OF DNA AND OTHER GENETIC RELATED SAMPLES**

**1. *Informed Consent Options:*** Subjects/patients should be given adequate information and options to help them understand clearly the nature of the decision they are about to make regarding collection, storage, and use of their biological materials when they agree to participate in a study. Depending on the nature of the study, investigators should always present subjects **option (a) and one** of the options (b-d) from the following list:

- a) Opt out – veteran declines use of their biological materials in research.
- b) Permit use of deidentified biological materials for the current study or for use in future studies, as consented.

- c) Permit use of identifiable biological materials. The PI must indicate
- by whom the samples are identifiable and where the key will be kept.
  - whether the samples will be kept at the VA or sent to a third (non-VA) party.  
Note: In cases involving a third party, identification must be possible only by a VA investigator, and the key containing the link to identifiers must be retained on a VA server.
  - whether the samples will be used only in the current study or in future studies.  
The VA IRB may allow creation of a DNA “bank” for identifiable/identified samples, and investigators will be expected to submit a protocol for review by the IRB prior to use. The consent form must state what purposes the biological materials will be used (only the health condition for which the sample was originally obtained, related health conditions, questions, or any kind of research).
  - whether future contact is permitted.
- d) Permit the use of identified specimens and samples. The investigator must demonstrate to the satisfaction of the IRB how they will (i) explain the risks to the veteran of this level of identification; and (ii) explain the scientific need for this level (as opposed to category b or c).

**2. Consent not Required for Additional Research on Deidentified And/or Unlinked Samples/specimens:**

Because the issues of confidentiality and privacy are of no concern in such instances, additional consent for deidentified or unlinked samples/specimens to be used in further research is not required.

**C. DISCLOSURE/PRIVACY OF RESEARCH RESULTS TO SUBJECTS/PATIENTS**

**1. Conditions for Disclosure**

Investigators should describe in the protocol and in the consent form anticipated research findings and circumstances that might lead to a decision to disclose findings to a subject/patient, as well as a plan for managing such disclosure.

Note to Investigators: Disclosure of research results to subject/patients should only occur when all of the following apply:

- a) The findings are scientifically valid and confirmed,
- b) The findings have significant implications for the subject/patients health concerns, and
- c) A course of action to ameliorate or treat these concerns is readily available.

If these criteria are met, consultation with the IRB must be made prior to disclosure.

**2. Privacy:**

It is expected that the researcher maintain patients/subjects privacy in conducting DNA and other genetic related information research. As far as practicable, separate records should be maintained on each patient/participant. Pedigrees and DNA samples should be coded so individuals working with samples or the database do not have access to personal information. In line with section B

above, it is required that no private genetic information about an individual member of a pedigree be provided to a 3rd party without that individual's authorization.

#### **D. RISKS**

Since the consent form will need to be placed in the chart, relevant risks should be clearly delineated as to the type of sample being collected. Potential risks may include:

**1. Social Risks:** Inform patients/participants that any breach of confidentiality could impact insurability, employability, reproduction plans, family relationships, immigration status, paternity suits, or stigmatization. Mention that VA healthcare benefits cannot be denied by the results of a genetic test. See below, section G.

**2. Psychological risks:** Inform patients/participants that if information is disclosed, psychological effects may result from learning the results of a test, learning that no effective therapy exists, or disclosing results to family members.

**3. Physical risks:** Inform patients/participants of physical risks associated with collecting samples (via blood draw, cheek swab, etc.).

**4. Unknown risks:** Inform patients/participants that there may be unknown risks. In addition, there may be future ramifications to patients/participants or their family members that are currently unclear/unknown.

#### **E. COSTS & AVAILABILITY OF COUNSELING**

Inform patients/participants of the availability and any costs of participation not covered by the study, such as the cost and location of genetic counseling or other counseling. (List specific genetic counseling or other counseling resources.)

#### **F. COMPENSATION**

Investigators should indicate whether veterans can receive monetary compensation as the result of any product or knowledge gained from the research.

#### **G. PROTECTION FROM DISCRIMINATION**

The Genetic Information Nondiscrimination Act (GINA) of 2008 prohibits health insurance companies from requiring or requesting genetic information of an individual or an individual's family members, or from using it to determine coverage, rates, or preexisting conditions. GINA also prohibits most employers (not employers < 15 employees) from using genetic information for hiring, firing, or promotion decisions. GINA does **not** prohibit underwriting altogether and does not protect from discrimination for life insurance, disability insurance, or long-term care insurance.

**GINA does not cover veterans.** Although existing publications indicate that the VA has separate policies to protect veterans, as of August 2011, the Office of General Counsel indicates that the VA has no specific policy addressing the use of genetic/genomic information due to the novelty of such issues. According to Renee Szybala, the former VBA Director of Compensation &

Pension Service, a genetic predisposition could never be considered a factor in determining whether or not a disease is service-connected (eligibility for benefits is discussed in Federal Regulations at 38 CFR Part 17). This view is confirmed in [(Vet. Aff. Op. Gen. Couns. 1-85, 1985 WL 1093098 (DVA) and VAOPGC 8-88 Vet. Aff. Op. Gen. Couns. 8-88 1988 WL 1532907 (DVA)] whereby: “An hereditary disease under 38 C.F.R. § 3.303(c) does not always rebut the presumption of soundness found in 38 U.S.C. §§ 311 and 332. Service connection may be granted for hereditary diseases which either first manifest themselves during service or which preexist service and progress at an abnormally high rate during service.” Accordingly, veterans may be reassured that they enjoy similar protection from discrimination as their civilian peers. The Office of General Counsel recommends that the following sentence be used in consenting veterans into genetic or genomic research: “VA has no policies that would deny benefits based on genetic information.”

Some veterans may have dual coverage by private insurance or Medicare. When the veteran is getting care from or participating in research at a VA facility, they are not covered by GINA. When the veteran is getting care from a non-VA facility, they are covered by GINA.

During the consent process, veterans should be made aware that their benefits cannot be affected by disclosure of genetic information that was obtained during a research study. If they ask specifically about GINA, they should be informed that they are not covered by GINA but that **“the VA has no specific policy that would deny benefits based on genetic information.”**

## **POSTSCRIPT**

The DVAMC Institutional Review Board is aware of the heightened sensitivity regarding several issues related to DNA and other genetic related information research (e.g., informed consent, confidentiality, privacy, tissue banking, etc.). Numerous entities are working to codify ethical principles regarding DNA and other genetic related information research to protect human subject/patients without unduly restricting potentially beneficial investigations.

Because such research is expanding rapidly with novel issues arising almost daily, it is not possible to propose a policy that applies to every research situation involving DNA and other genetic-related information. Further, all research, including DNA and other genetic-related information investigation, involves a significant level of trust between sponsor and institution, investigator and patient/participant, and investigator and IRB.

In light of these factors, it is the recommendation of the DVAMC IRB that investigators follow the guidance presented above regarding DNA and other genetic information research. Although all research submitted to the IRB is considered on a case-by-case basis, these guidelines will provide help to investigators preparing protocols for research involving DNA and other genetic related information. This guide will also be a reference for the IRB in considering DNA and other genetic-related information related research protocols submitted to it.

## **SELECTED ON LINE RESOURCES**

NIH has a catalogue of bioethics sites at: [www.nih.gov/sigs/bioethics/](http://www.nih.gov/sigs/bioethics/)

HGPI: Human Genome Project Information site has the ELSI (Ethical Legal and Social Issues) documents. [www.ornl.gov/sci/techresources/Human\\_Genome/elsi/elsi.shtml](http://www.ornl.gov/sci/techresources/Human_Genome/elsi/elsi.shtml)

NBAC: Home page for the National Bioethics Advisory Commission is found at either:  
[www.bioethics.gov/](http://www.bioethics.gov/)

American Society for Bioethics + Humanities  
[www.asbh.org](http://www.asbh.org)

National Human Genome Research Institute (National Institutes of Health)  
[www.genome.gov](http://www.genome.gov)

The Genetic Privacy Act: A model law developed by the Boston University School of Health, ELSI and DOE. [www.ornl.gov/hgmis/resource/privacy/privacy1.html](http://www.ornl.gov/hgmis/resource/privacy/privacy1.html)

Question and answer session about GINA:  
[www.dnapolicy.org/resources/RFIanalysis.pdf](http://www.dnapolicy.org/resources/RFIanalysis.pdf)

Genetic Information Nondiscrimination Act of 2008  
<http://www.genome.gov/Pages/PolicyEthics/GeneticDiscrimination/GINAInfoDoc.pdf>

HUGO: The Human Genome Organization (international) has a “Statement on DNA Sampling: Control and Access” by the Ethics committee of HUGO listing seven recommendations re: 1) potential uses; 2) routine samples; 3) research samples; 4) security; 5) access by relatives; 6) disclosure and 7) standardization of procedures.  
[http://www.hugo-international.org/img/dna\\_1998.pdf](http://www.hugo-international.org/img/dna_1998.pdf) “Survey of Informed Consents” by Dorothy C. Wertz. An abstract of a study done by Robert F. Weir (Univ of Iowa) indicating percentages of consent forms that include/omit important items in DNA related consent forms. It is in “The Gene Letter” Vol. 1, Issue 4, January 1997. [www.geneletter.org](http://www.geneletter.org)

Salvaterra E, Lecchi L, Giovanelli S, et al. (2008) Banking together. European Molecular Biology Organization Reports 9(4), 307-313.

Baruch S & Hudson K. (2008) Civilian and military genetics: Nondiscrimination policy in a post-GINA world. American Journal of Human Genetics 83, 435-444.

## **REGULATORY REFERENCES**

These guidelines should not be construed to differ from, or substitute for, the regulations or policies and procedures of appropriate regulatory agencies such as:

DVA: Dept of Veterans Affairs 38 CFR 16

DHHS: Federal Regulations for the Protections of Human Subjects 45 CFR 46

DHHS: Office for Human Research Protections (OHRP)  
ORD: Office of Research and Development (VA)

These guidelines are intended to supplement regulatory policies and procedures by focusing on issues of informed consent, privacy and confidentiality, etc., in studies involving DNA research which the DVAMC Human Studies Subcommittee is responsible to interpret and apply in reviewing proposals submitted to it. These guidelines may be revised as conditions warrant. Suggestions from investigators to the Chair of the DVAMC Human Studies Subcommittee or the ACOS/R are welcome.

### ***SUPPLEMENTAL REFERENCES***

In addition to the above regulatory references, several advisory agencies interpret, expand, and make recommendations regarding ethical issues involving DNA research. The principal ones (referred to in) developing these guidelines [in alphabetical order] are:

ARENA: American Research Ethics National Association  
ELSI: Ethical, Legal, and Social Issues of the Human Genome Project  
GENETIC INFORMATION NONDISCRIMINATION ACT  
NBAC: National Bioethics Advisory Commission (Report and Recommendations  
August 1999, Volume 1, "Research Involving Human Biological Materials:  
Ethical Issues and Policy Guidance")